PTO/SB/21 (09-04)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# TRANSMITTAL FORM

*(to be used for all correspondence after initial filing)*

Total Number of Pages in This Submission | 11

| | |
|---|---|
| Application Number | 09/849,022 |
| Filing Date | May 4, 2001 |
| First Named Inventor | Joseph D. Gold, et al. |
| Art Unit | 1632 |
| Examiner Name | Thaian N. Ton |
| Attorney Docket Number | 091/005P |

## ENCLOSURES *(Check all that apply)*

- [x] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation
- [ ] Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] Appeal Communication to TC
  - [x] Appeal Brief (8 pages)
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please identify below):
  (___ pages)

Remarks

***last page marker (1 page)***

RECEIVED
JUN - 8 2005
OIPE / IAP

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | | | |
|---|---|---|---|
| Firm Name | Geron Corporation | | |
| Signature | | | |
| Printed name | J. Michael Schiff | | |
| Date | June 7/05 | Reg. No. | 40,253 |

## CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

| | | | |
|---|---|---|---|
| Signature | Karen Zielen | | |
| Typed or printed name | Karen Zielen | Date | June 7, 2005 |

PTO/SB/17 (12-04v2)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE


*Effective on 12/08/2004.*
*Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).*

# FEE TRANSMITTAL For FY 2005

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 250

| Complete If Known | |
|---|---|
| Application Number | 09/849,022 |
| Filing Date | May 4, 2001 |
| First Named Inventor | Joseph D. Gold, et al. |
| Examiner Name | Thalan N. Ton |
| Art Unit | 1632 |
| Attorney Docket No. | 091/005P |

**METHOD OF PAYMENT** (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☑ Deposit Account Deposit Account Number: 07-1139 Deposit Account Name: Geron Corporation

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☑ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee

☑ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☑ Credit any overpayments

**WARNING:** Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

**FEE CALCULATION**

**1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

| Application Type | FILING FEES Fee ($) | FILING FEES Small Entity Fee ($) | SEARCH FEES Fee ($) | SEARCH FEES Small Entity Fee ($) | EXAMINATION FEES Fee ($) | EXAMINATION FEES Small Entity Fee ($) | Fees Paid ($) |
|---|---|---|---|---|---|---|---|
| Utility | 300 | 150 | 500 | 250 | 200 | 100 | |
| Design | 200 | 100 | 100 | 50 | 130 | 65 | |
| Plant | 200 | 100 | 300 | 150 | 160 | 80 | |
| Reissue | 300 | 150 | 500 | 250 | 600 | 300 | |
| Provisional | 200 | 100 | 0 | 0 | 0 | 0 | |

**2. EXCESS CLAIM FEES**

| Fee Description | Fee ($) | Small Entity Fee ($) |
|---|---|---|
| Each claim over 20 (including Reissues) | 50 | 25 |
| Each independent claim over 3 (including Reissues) | 200 | 100 |
| Multiple dependent claims | 360 | 180 |

Total Claims _____ - 20 or HP = _____ x _____ = _____ Fee Paid ($)
HP = highest number of total claims paid for, if greater than 20. total claims previously paid = 44

Indep. Claims _____ - 3 or HP = _____ x _____ = _____ Fee Paid ($)
HP = highest number of independent claims paid for, if greater than 3. total independent claims previously paid = 4

Multiple Dependent Claims Fee ($) _____ Fee Paid ($) _____

**3. APPLICATION SIZE FEE**

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets _____ - 100 = _____ Extra Sheets _____ / 50 = _____ Number of each additional 50 or fraction thereof (round up to a whole number) x Fee ($) _____ = Fee Paid ($) _____

**4. OTHER FEE(S)**

Fees Paid ($)

Non-English Specification, $130 fee (no small entity discount) _____

Other (e.g., late filing surcharge): Appeal Brief 250

**SUBMITTED BY**

| | | | |
|---|---|---|---|
| Signature | | Registration No. (Attorney/Agent) 40,253 | Telephone (650) 473-7715 |
| Name (Print/Type) | J. Michael Schiff | | Date June 7/05 |

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

RECEIVED
CENTRAL FAX CENTER

JUN 0 7 2005

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being transmitted to the U.S. Patent & Trademark Office in accordance with 37 CFR § 1.6(d) on the date indicated.

Karen Zieler
Name

June 7, 2005
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| Inventors: Joseph Gold et al. | Art Unit: 1632 |
| Filing Date: May 4, 2001 | Examiner: Thái-An N. Ton, Ph.D. |
| Serial No: 09/849,022 | |
| Docket: 091/005p | |
| Title: GENETICALLY ALTERED HUMAN PLURIPOTENT STEM CELLS | |

**APPEAL BRIEF**

Commissioner for Patents
Alexandria VA 22313

Dear Sir,

This paper is subsequent to the Amendment and Response filed in this application under 37 CFR § 1.116 on September 10, 2004, April 7, 2005, and May 13, 2005. A Notice of Appeal was filed in this application on November 8, 2004, setting the deadline for filing an Appeal Brief to January 8, 2004. The time for filing an Appeal Brief was extended on May 13, 2005 by five months, setting the deadline to June 8, 2005. Accordingly, this Appeal Brief is timely filed.

The effect of this paper *inter alia* is to extend the pendency of this application and give applicant and the Examiner a further opportunity to put the application in condition for allowance.

06/08/2005 SFELEKE1 00000043 071139 09849022
01 FC:2402 250.00 DA

## PENDING CLAIMS

1. *(Previously presented)* A method for producing a population of genetically altered human embryonic stem (hES) cells, comprising:

   a) obtaining a population of hES cells essentially free of feeder cells; and

   b) transfecting the cells with a polynucleotide while being cultured on an extracellular matrix in a medium conditioned by fibroblast feeder cells, wherein the polynucleotide comprises a protein encoding region operably linked to a promoter that promotes transcription of the encoding region while the cells are undifferentiated,

   thereby producing genetically altered hES cells that express the protein while undifferentiated.

2. *(Original)* The method of claim 1, further comprising preferentially selecting cells that have been genetically altered with the polynucleotide.

3. *(Previously presented)* The method of claim 1, wherein the human embryonic stem cells are maintained in an environment comprising extracellular matrix components and a conditioned medium produced by collecting medium from a culture of feeder cells.

4 & 5. *CANCELLED*

6. *(Previously presented)* The method of claim 1, wherein the polynucleotide is selected from an adenoviral vector, a retroviral vector, and a DNA plasmid complexed with positively charged lipid.

7. *CANCELLED*

8. *(Previously presented)* A cell population comprising undifferentiated human embryonic stem (hES) cells cultured on an extracellular matrix in a medium conditioned by fibroblast feeder cells,

   wherein the population comprises cells expressing a protein from a heterologous polynucleotide in which an encoding region for the expressed protein is operably linked to a promoter that promotes transcription of the encoding region while the hES cells are undifferentiated.

9. *(Previously presented)* A cell population comprising undifferentiated hES cells cultured on an extracellular matrix in a medium conditioned by fibroblast feeder cells,

wherein the population comprises cells stably transfected so as to express a protein from a heterologous polynucleotide in which an encoding region for the expressed protein is operably linked to a promoter that promotes transcription of the encoding region while the hES cells are undifferentiated.

10 to 12. *CANCELLED*

13. *(Previously presented)* The cell population of claim 8, in which at least 90% of the undifferentiated hES cells have been genetically altered.

14. *CANCELLED*

15. *(Previously presented)* The cell population of claim 9, in which at least 90% of the undifferentiated hES cells have been stably transfected.

16. *(Previously presented)* A method for producing genetically altered differentiated cells, comprising differentiating the cells of claim 9.

17. *(Previously presented)* A method for producing genetically altered differentiated cells, comprising:

a) obtaining a population of hES cells essentially free of feeder cells and maintained on an extracellular matrix in a medium conditioned by fibroblast feeder cells; and

b) transfecting at least some of the cells in the composition with a polynucleotide, thereby producing genetically altered cells; and

c) causing the genetically altered cells to differentiate into a population of neural cells or hepatocytes.

18. *(Previously presented)* The method of claim 16, whereby the genetically altered cells are differentiated into neural cells.

19. *(Previously presented)* The method of claim 16, whereby the genetically altered cells are differentiated into hepatocytes.

20. *(Previously presented)* The method of claim 17, whereby the differentiated cell population is over 50% neural cells.

21. *(Previously presented)* The method of claim 17, whereby the differentiated cell population is over 50% hepatocytes.

22. *(Previously presented)* The method of claim 1, wherein the polynucleotide encodes a drug resistance gene.

23. *(Previously presented)* The method of claim 2, wherein the selecting comprises culturing the cells in the presence of a drug to which genetically altered cells in the population are resistant.

24. *(Previously presented)* The method of claim 1, wherein said promoter is selected from the EF1a promoter and the PGK promoter.

25. *(Previously presented)* The cell population of claim 8, wherein said promoter is selected from the EF1a promoter and the PGK promoter.

26. *(Previously presented)* The cell population of claim 9, wherein said promoter is selected from the EF1a promoter and the PGK promoter.

27. *(Previously presented)* The cell population of claim 8, which consists of human cells.

28. *(Previously presented)* The cell population of claim 9, which consists of human cells.

29. *(Previously presented)* The cell population of claim 8, wherein the protein is a factor that supports growth of the hES cells.

30. *(Previously presented)* The cell population of claim 29, wherein the protein is a fibroblast growth factor.

31. *(Previously presented)* The cell population of claim 8, wherein the protein is a detectable label.

32 *(Previously presented)* The cell population of claim 31, wherein the label is a fluorescent label.

33. *(Previously presented)* The cell population of claim 32, wherein the label is selected from luciferase and green fluorescent protein (GFP).

34. *(Previously presented)* The cell population of claim 31, wherein the label is a cell surface protein detectable by antibody staining.

35. *(Previously presented)* The cell population of claim 31, wherein the label is an enzyme.

36. *(Previously presented)* The cell population of claim 35, wherein the label is selected from alkaline phosphatase, β-galactosidase, and neophosphotransferase.

## REMARKS

This paper is subsequent to the Amendment and Response filed in this application under 37 CFR § 1.116 on September 10, 2004, April 7, 2005, and May 13, 2005.

The effect of this paper *inter alia* is to extend the pendency of this application and give applicant and the Examiner a further opportunity to put the application in condition for allowance.

Further consideration and allowance of the application is respectfully requested.

Rejections under 35 USC § 112 ¶ 1:

The pending claims stand rejected under the enablement requirement of § 112 ¶ 1. The Office Action of June 10, 2004, indicates that the specification is enabling for methods of obtaining or producing genetically altered hES cells in the absence of feeder cells on an extracellular matrix in a medium conditioned by feeder cells.

The claims are herein amended as recommended by the Examiners. The cells are explicitly involve culturing the hES cells *on an extracellular matrix in a medium conditioned by fibroblast feeder cells.*

Accordingly the rejection made in the previous Office Action is moot. Applicant maintains that the application as filed is enabling for further methods of making genetically modified cells, coverage for which will be pursued in a related application.

Claims 17-21 relate to hES cells differentiated into populations of neurons or hepatocytes. The present application as filed describes a method for differentiating hES cells into populations comprising over 90% neural cells (page 20, lines 18-31). This is an embodiment of the method described in U.S. Patent 6,833,269 and its priority application, filed May 17, 2000. The present application as filed also describes a method for differentiating hES cells into populations comprising over 80% hepatocyte lineage cells (page 20, line32 to page 21, line 2). This is an embodiment of the method described in U.S. Patent 6,458,589 and its priority application, filed April 27, 2000.

Withdrawal of the rejection under § 112 ¶ 1 is respectfully requested.

Double Patenting

Certain claims in this application were rejected for obviousness type double patenting over claims 62 and 63 of USSN 09/530,346. This application has since been issued as U.S. Patent 6,800,480. The corresponding claims in the issued patent are claims 10 and 11.

The reason given for this rejection in the January 16, 2004 Office Action is that the method claims in the present application are the only way of making the genetically altered cells in the 6,800,480 patent.

Applicants respectfully submit that this rejection is also moot in view of the amendments to the claims made before and herein. The 6,800,480 patent does not explicitly claim genetically altered cells cultured on an extracellular matrix in a medium cultured by fibroblast feeder cells. There are certainly other ways of making genetically altered pPS cells. For example:

- hES cells can be transfected with such agents as Lipofectamine 2000™ and FuGene™ while being cultured on a feeder layer of normal primary mouse fibroblasts. This is illustrated in the specification in Example 3.
- hES cells can be grown on a layer of feeder cells made to be drug resistant, genetically altered, and then selected using the corresponding antibiotic. This is exemplified in the specification in Example 5, and previously presented in claim 4, which has since been cancelled.
- hES cells can also be genetically altered in other feeder-free culture systems. For example, US 2003/0017589 A1 describes a feeder-free system using non-conditioned medium, and its use for making genetically altered cells.

Since the genetically altered cells in the 6,800,480 patent can be made by methods other than those in the claims as presented above, the claims are not obvious over the claims in the issued patent. Accordingly, no Terminal Disclaimer is needed

Furthermore, a Terminal Disclaimer was filed with respect to the '480 patent on May 13, 2005.

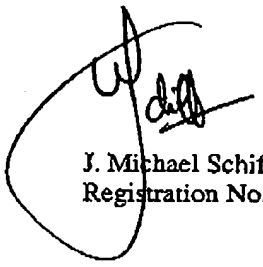
PATENT
09/849,022
Docket 091/005

Fees Due

Accompanying this Amendment are papers authorizing the Commissioner to charge the fee for the Appeal Brief and the extension of time to applicant's deposit account.

Should the Patent Office determine that an extension of time or any other relief is required for further consideration of this application, applicant hereby petitions for such relief, and authorizes the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



J. Michael Schiff
Registration No. 40,253

GERON CORPORATION
230 Constitution Drive
Menlo Park, CA 94025
*Telephone: (650) 473-7715*
*Fax: (650) 473-8654*

June 8, 2005

geron

GERON CORPORATION
230 Constitution Drive
Menlo Park, CA 94025
Phone: (650) 473-7700
Fax: (650) 473-8654

*Facsimile Transmittal Sheet*

# LAST PAGE

## USSN 09/849,022

## Attorney Docket 091/005P